IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : David Lew Simon

App. Ser. No. : 10/628,089

Filed : July 25, 2003

For : "Improved Opioid Pharmaceutical Compositions"

Art Unit : 1614

Examiner :

DISCLOSURE OF TWO ADDITIONAL UNITED STATES PATENTS AND TRANSMITTAL OF REVISED PTO-1449 DISCLOSURE FORM PRIOR TO EXAMINATION

Commissioner of Patents and Trademarks
P.O. Box 1450
Alexandria, VA 22313

Sir:

Since the time the above-referenced patent application was filed, Applicant has unexpectedly discovered two additional references that Applicant believes the Examiner may want to review relating to the pending patent application; the additional references are U.S. Patent Nos. 4,366,159 and 4,464,378, copies of which accompany this letter. In addition, a revised document disclosure Form 1449, reflecting the two additional patents, is enclosed. Applicant does not believe the additional documents will have an adverse impact on pending patent application Ser. No. 10/628,089, and submits the additional documents in the spirit of full disclosure and in compliance with *37 CFR 1.56*.

Respectfully submitted,

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Form PTO-1449 Modified
List of Patents & Publications Cited by Applicant
U.S. Dept. of Commerce
Patent & Trademark Office

		Serial No. 10/628,089
	Inventor: David Lew Simon	
		Filing Date: 7/25/2003
	Title: "Improved Opioid Pharmaceutical Compositions"	
	Other Documents (Including Author, Title, Date, Pertinent Pages, etc.)	

In order of appearance in the Specifications:

	Document	Author/Title/Journal	Pages
	AA	Drawing marked "Figure 1" from Opioid Peptides in Substance Abuse by Jozsef I. Szekely, ISBN 0-8493-7937-7.	160
	AB	Spanagel, R., et al., "Opposing tonically active endogenous opioid systems modulate the mesolimbic dopaminergic pathway," Proc. Natl. Acad. Sci. USA, Vol. 89 pp. 2046-2050, March 1992.	2046 [see Abstract]
	AC	Pan, Z. Z., et al., "Cellular mechanism for anti-analgesic action of agonists of the *k*-opioid receptor," Nature, Vol. 389 pp. 382-385, September 25, 1997.	382
	AD	Culpepper-Morgan J. A., et al., "Orally administered opioid antagonists reverse both mu and kappa opioid agonist delay of gastrointestinal transit in the guinea pig," Life Sciences, Vol. 56, No. 14, pp. 1187-1192, 1995. [Referenced as "Kreek et al.]	1187 [see Summary]
	AE	Arts, K. S. et al., "Inhibition of the Antianalgesic Action of Dynorphin A in Mice by Cholera Toxin," Pharmacology, Biochemistry and Behavior, Vol. 46, pp. 623-629, 1993. [Referenced as "Fujimoto, et al."]	623 [see Abstract]
	AF	Bakshi, R. et al., "Dynorphin A-(1-17) Induces Alterations in Free Fatty Acids, Excitatory Amino Acids, and Motor Function Through An Opiate-Receptor-Mediated Mechanism," The Journal of NeuroScience, Vol. 10, No. 12, pp. 3793-3800, December 1990.	3793 [see Abstract]
	AG	Behrmann, D. L., et al. "A Comparison of YM-14673, U-50488H, and Nalmefene after Spinal Cord Injury in the Rat," Experimental Neurology, Vol.	258

	Document	Author/Title/Journal	Pages
		119, pp. 258-267, 1993.	
	AH	Ohnishi et al., "Aquaretic Effect of the Stable Dynorphin-A Analog E2078 in the Human," The Journal of Pharmacology and Experimental Therapeutics, Vol. 270, No. 1, pp. 342-347, 1994.	342
	AI	Ranade V. V. & Hollinger, M. A., Chapter 8 "Miscellaneous Forms of Drug Delivery" in Drug Delivery Systems, ISBN 0-8493-8542-3, 1996.	287
	AJ	Hatefi, A. & Amsden, B., "Review: Biodegradable injectable in situ forming drug delivery systems," Journal of Controlled Release, Vol. 80, pp. 9-28, 2002.	*En toto*
	AK	Tarr, B. D. et al., "A new parenteral emulsion for the administration of taxol," Pharm Res, Vol. 4, No. 2, pp. 162-5, April 1987 [Abstract].	See Abstract
	AL	Bailey, J. W. et al., "Calcium, magnesium, and phosphorus metabolism in dogs given intravenous triacetin," Am J Clin Nutr, Vol. 49, No. 2, pp.385-8, Feb. 1989 [Abstract].	See Abstract
	AM	Bailey, J. W. et al., "Triacetin: a potential parenteral nutrient," JPEN J Parenter Enteral Nutr, Vol. 15, No. 1, pp. 32-6, Jan-Feb 1991 [Abstract].	See Abstract
	AN	Karlstad, M.D., et al., "Parenteral nutrition with short- and long-chain triglycerides: triacetin reduces atrophy of small and large bowel mucosa and improves protein metabolism in burned rats," Am J Clin Nutr, Vol. 55, No. 5, pp. 1005-11, May 1992 [Abstract].	See Abstract
	AO	Bleiberg, B. et al., "Metabolism of triacetin-derived acetate in dogs," Am J Clin Nutr, Vol. 58, No. 6, pp. 908-11, Dec 1993 [Abstract].	See Abstract
	AP	Gekker, G. et al., "Naltrexone potentiates anti-HIV-1 activity of antiretroviral drugs in CD4+ lymphocyte cultures," Drug and Alcohol Dependence, Vol. 64, pp. 257-263, 2001.	257 [see Abstract]
	AQ	Li, Y. et al., "Methadone enhances human immunodeficiency virus infection of human immune cells," J Infect Dis, Vol. 185, No. 1, pp. 118-22, Jan 1, 2002.	118 [see Abstract]
	AR	Mahayni, H. & Minor, J. R., "Antiretroviral activity of naloxone and naltrexone," Am J Hosp Pharm, Vol. 48, No. 11, pp. 2480-1, Nov 1991 [Letter].	2480-2481

	AS	Bihari, B., "Efficacy of low dose naltrexone as an immune stabilizing agent for the treatment of HIV/AIDS," AIDS Patient Care, Vol. 9, No. 1, p. 3, Feb 1995 [Letter].	3
	AT	Schluger, J. H., et al., "Nalmefene causes greater hypothalamic-pituitary-adrenal axis activation than naloxone in normal volunteers: implications for the treatment of alcoholism," Alcohol Clin Exp Res, Vol. 22, No. 7, pp. 1430-6, Oct 1998.	1430 [Abstract], 1434 & 1435
	AU	Suzuki, S. et al., "Morphine upregulates kappa-opioid receptors of human lymphocytes," Adv Exp Med Biol, Vol. 493, pp. 81-7, 2001.	81 [see Abstract]
	AV	Smetnev, A. S., et al. "Diagnostic value of diurnal ECG monitoring, the bicycle exercise test and intracardiac electrophysiological study in the detection of arrhythmia in patients with alcoholic lesions of the heart [in Russian], Ter Arkh, Vol. 60, No. 1, pp. 49-51, 1988 [Abstract].	See Abstract
	AW	Faintuch, J. J., "Cardiovascular impact of alcoholism," Rev Hosp Clin Fac Med Sao Paulo, Vol. 50, No. 1, pp. 76-9, Jan-Feb 1995 [Abstract].	See Abstract
	AX	Fabrizio, L. & Regan, T. J., "Alcoholic cardiomyopathy," Cardiovasc Drugs Ther, Vol. 8, No. 1, pp. 89-94, Feb 1994 [Abstract].	See Abstract
	AY	Nakamura, K., et al., "Increase in beating rate of cultured chick cardiac myocytes by ethanol and inhibition by antiarrhythmic drugs," Alcohol Clin Exp Res, Vol. 23 (4 Suppl), pp. 81S-84S, Apr 1999 [Abtract].	See Abstract
	AZ	Ettinger, P. O., et al., "Cardiac conduction abnormalities produced by chronic alcoholism," American Heart Journal, Vol. 91, No. 1, pp. 66-78, Jan 1976.	66
	BA	Caldwell, R. W., et al. "Actions of the opioid antagonist, nalmefene, and congeners on reperfusion cardiac arrythmias and regional left coronary blood flow," Pharmacology, Vol. 41, No. 3, pp. 161-6, 1990.	161 [see Abstract]
	BB	Wang, D., et al., "Inverse agonists and neutral antagonists at mu opioid receptor (MOR): possible role of basal receptor signaling in narcotic dependence," J Neurochemistry, Vol. 77, No. 6, pp. 1590-600, June 2001.	1591, 1592, 1594, 1598, 1599.

Examiner's initials	Document	Author/Title/Journal	Pages
	BC	Gharagozlou, P, et al., "Activity of opioid ligands in cells expressing cloned mu opioid receptors," BMC Pharmacology, Vol. 3, pp. 1-8, January 4, 2003	See Abstract; Column 2, page 2; Page 3, tables 1 & 2; Page 4, fig. 1; Page 5
	BD	Yoburn, BC, et al., "Supersensitivity to opioid analgesics following chronic opioid antagonist treatment: relationship to receptor selectivity," Pharmacology Biochemistry and Behavior, Vol. 52, Nos. 2/3, pp. 535-539, June-July 1995.	See Abstract
	BE	Paronis, CA and Holtzman, SG, "Increased analgesic potency of mu agonists after continuous naloxone infusion in rats," The Journal of Pharmacology and Experimental Therapeutics, Vol. 259, No. 2, pp. 582-9, November, 1991.	See Abstract
	BF	Liu, J and Prather, PL, "Chronic Exposure to mu-Opioid Agonists Produces Constitutive Activation of mu-Opioid Receptors in Direct Proportion to the Efficacy of the Agonist Used for Pretreatment," Molecular Pharmacology, Vol. 60, No. 1, pp. 53-62, 2001.	See Abstract
	BG	Rukstalis, MR, et al., "6-beta-naltrexol reduces alcohol consumption in rats," Alcoholism Clinical and Experimental Research, Vol. 24, No. 10, pp 1593-96, October 2000.	*En toto*
	BH	Weinhold, LL, et al., "Buprenorphine Alone and in Combination with Naltrexone in Non-Dependent Humans," Drug and Alcohol Dependence, Vol. 30, pp. 263-274, 1992.	[Abstract only]
	BI	Mendelson, J, et al., "Buprenorphine and Naloxone Interactions in Opiate-Dependent Volunteers," Clin Pharm Ther, Vol. 60, pp.105-114, 1996.	[Abstract only]

Examiner's initials	Document	Author/Title/Journal	Pages
	BJ	Remington's Pharmaceutical Sciences (Arthur Osol, editor).	
	BK	Physicians' Desk Reference, 54th Edition, 2000.	974; 3132;
	BL	Porter, SJ, et al., "Kinetics and inhibition of the formation of 6beta-naltrexol from naltrexone in human liver cytosol," British Journal of Clinical Pharmacology, Vol. 50, pp. 465-472, 2000	See Abstract
	BM	Ferrari, A, et al., ""Serum time course of naltrexone and 6beta-naltrexol levels during long-term treatment in drug addicts," Drug and Alcohol Dependence, Vol. 52, pp. 211-220, 1998.	See Abstract; pp. 216-217, figures 2 and 3
	BN	Porter, SJ, et al., "In vivo and in vitro potency studies of 6-beta naltrexol, the major human metabolite of naltrexone," Addiction Biology, Vol. 7, No. 2, pp. 219-225, April 2002.	[Abstract only]
	BO	Lukas, SE, et al., "EEG alpha activity increases during transient episodes of ethanol-induced euphoria," Pharmacology Biochemistry and Behavior, Vol. 25, No. 4, pp. 889-95, October, 1996.	[Abstract only]
	BP	Lukas, SE, et al., "Electroencephalographic correlates of marihuana-induced euphoria," Drug and Alcohol Dependence, Vol. 37, no. 2, pp. 131-40, February 1995.	[Abstract only]
	BQ	Chang, PF, et al., "Differential cerebral responses to aversive auditory arousal versus muscle pain: specific EEG patterns are associated with human pain processing," Exp Brain Res, Vol. 147, No. 3, pp. 387-93, December 2002.	[Abstract only]
	BR	Chang, PF, et al., "Psycophysical and EEG responses to repeated experimental muscle pain in humans: pain intensity encodes EEG activity," Brain Res Bull., Vol. 59, No. 6, pp. 533-43, February 2003.	[Abstract only]
	BS	Ross, FB and Smith MT, "The intrinsic antinociceptive effects of oxycodone appear to be kappa-opioid receptor mediated," Pain, Vol. 73, No. 2, pp.151-7, November, 1997	[Abstract only]

Examiner's initials	Document	Author/Title/Journal	Pages
	BT	Kaiko, R, et al., "Pharmacokinetic-pharmacodynamic relationships of controlled-release oxycodone," Clinical Pharmacology and Therapeutics, Vol. 59, No. 1, pp. 52-61, January 1996.	See Abstract
	BU	Abbruscato, TJ, et al., "Blood-Brain Barrier Permeability and Bioavailability of a Highly Potent an mu-Selective Receptor Antagonist, CTAP: Comparison with Morphine," The Journal of Pharmacology and Experimental Therapeutics, Vol. 28, No. 1, pp. 402-409, 1997,	Page 403, first column, last paragraph

The following documents are not specifically referenced in the Specifications, but are generally germane to the technologies discussed and are included for completeness' sake:

Examiner's initials	Document	Author/Title/Journal	
	BV	Seven page FAX from Dr. Alison Oliveto at Yale University/VAMC, describing the ARCI and POMS rating instruments	
	BW	McMahon, LR, et al., "Relative efficacy of buprenorphine, nalbuphine and morphine in opioid-treated rhesus monkeys discriminating naltrexone," Journal of Pharmacology and Experimental Therapeutics, Published May 23, 2003.	
	BX	Liu, J and Prather, PL, "Chronic Agonist Treatment Converts Antagonists into Inverse Antagonists at delta-Opioid Receptors," The Journal of Pharmacology and Experimental Therapeutics, Vol. 302, No. 3, pp. 1070-79, 2002.	
	BY	Stromberg, MF, et al., "A comparison of the effects of 6-beta naltrexol and naltrexone on the consumption of ethanol or sucrose using a limited-access procedure in rats," Pharmacology Biochemistry and Behavior, Vol. 72, Nos. 1-2, pp. 483-90, May 2002.	

	BZ	Morris, BJ and Millan, MJ, "Inability of an opioid antagonist lacking negative intrinsic activity to induce opioid receptor up-regulation in vivo," pp. 883-886 (unspecified journal)	
	CA	Loew, KP and Smith MT, "The antinociceptive potencies of oxycodone, noroxycodone and morphine after intracerbroventricular administration in rats," Life Sciences, Vol. 54, No. 17, pp. 1229-36, 1994. [Abstract only]	
	CB	Skarke, C, et al., "Analgesic effects of morphine and morphine-6-glucuronide in a transcutaneous electrical pain model in healthy volunteers," Clinical Pharmacology and Therapeutics, Vol. 73, No. 1, pp. 107-21, January 2003.	

	Document	U.S. Patent No. or Application Serial No. / First Named Inventor	Pages
	1	4,626,539 / Aungst	*En toto*
	2	5,512,593 / Dante	*En toto*
	3	5,580,876 / Crain [Abstract]	
	4	5,633,000 / Grossman [Abstract]	
	5	5,767,125 / Crain [Abstract]	
	6	5,783,583 / Simon	*En toto*
	7	5,972,954 / Foss [Abstract]	
	8	6,103,258 / Simon	*En toto*
	9	6,277,384 / Kaiko [Abstract]	
	10	6,475,494 / Kaiko [Abstract]	
	11	20010002259-A1 / Reder [Abstract]	
	12	20010049375-A1 / Sadee [Abstract]	
	13	20030069262-A1 / Sadee [Abstract]	
	14	10/127,385 / Simon	
	15	4,366,159 / Magruder	*En toto*
	16	4,464,378 / Hussain	*En toto*

EXAMINER DATE CONSIDERED

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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.